CLAIMS:

1. A method for detecting or determining one or more forms of Factor XIIa in a sample, which comprises carrying out a procedure that is capable of detecting or determining the form or forms of Factor XIIa under investigation in preference to other forms of Factor XIIa.

2. A method as claimed in claim 1, which comprises detecting or determining the form or forms of Factor XIIa under investigation by means of an assay that enables determination of the form or forms of Factor XIIa under investigation in preference to other forms of Factor XIIa.

3. A method as claimed in claim 1, which method comprises separating the form or forms of Factor XIIa under investigation from other forms of Factor XIIa and detecting or determining the separated form or forms of Factor XIIa.

4. A method as claimed in claim 3, wherein the detection or determination of the separated form or forms of Factor XIIa is by means of an assay as defined in claim 2.

5. A method as claimed in claim 1, which comprises contacting the sample with a labeled antibody that is capable of binding to the form or forms of Factor XIIa under investigation and that is optionally also capable

of binding to other forms of Factor XIIa, separating the form or forms of Factor XIIa under investigation from other form, and detecting or determining the form or forms of Factor XIIa under investigation.

6. A method as claimed in any one of claims 3 to 5, wherein the form or forms of Factor XIIa under investigation is/are separated from other forms of Factor XIIa on the basis of the physical, chemical or immunological properties thereof.

7. A method as claimed in claim 6, wherein the form or forms of Factor XIIa under investigation is/are separated from other forms of Factor XIIa using a chromatographic, flow cytometric or ultracentrifugation procedure, optionally followed by assessment of the enzymatic activity or immunological properties of the separated material.

8. A method as claimed in claim 6, wherein the form or forms of of Factor XIIa under investigation is/are separated by immunoaffinity chromatography using an antibody capable of binding to the form or forms of Factor XIIa under investigation, optionally followed by assessment of enzymatic activity or immunological properties of the separated material.

9. A method as claimed in claim 7 or claim 8, wherein the separation procedure is carried out under conditions such that the form or forms of Factor XIIa is/are not disrupted.

10. A method as claimed in any one of claims 1 to 9, wherein the sample is a sample of a body fluid or body tissue.

11. A method as claimed in claim 10, wherein the body fluid is blood, plasma or serum.

12. A method as claimed in claim 10, wherein the body fluid is urine, cerebrospinal fluid, saliva, or tears.

13. A method as claimed in any one of claims 1 to 12, wherein the form of Factor XIIa under investigation is cellular Factor XIIa.

14. A method as claimed in any one of claims 3 to 12, wherein the form of Factor XIIa under investigation is cellular Factor XIIa, which cellular Factor XIIa is separated from other forms of Factor XIIa by separating cells, cell remnants and/or cellular material from the liquid phase of a body fluid or from tissue.

15. A method as claimed in claim 14, wherein cells, cell remnants and/or cellular material are separated by centrifugation.

16. A method as claimed in any one of claims 13 to 15, wherein cellular Factor XIIa is separated from other Forms of Factor XIIa before detection or determination of Factor XIIa.

17. A method as claimed in any one of claims 1 to 12, wherein the form of Factor XIIa under investigation is lipid bound Factor XIIa.

18. A method as claimed in claim 17, wherein the form of Factor XIIa under investigation is lipid bound Factor XIIa, which lipid bound Factor XIIa is separated from non-lipid bound Factor XIIa by isolating a lipid fraction from the body fluid or the tissue.

19. A method as claimed in claim 18, wherein the lipid fraction comprises lipoproteins and/or remnants thereof.

20. A method as claimed in claim 19, wherein the lipid fraction is precipitated using a lipoprotein precipitation agent.

21. A method as claimed in any one of claims 17 to 20, wherein lipid bound factor XIIa is contacted with a labeled antibody before the lipid bound Factor XIIa is separated from other forms of Factor XIIa.

22. A method as claimed in any one of claims 1 to 12, wherein the form or forms of Factor XIIa under investigation is any one or more of complexes comprising two or more molecules of Factor XIIa, Factor XIIa associated with low affinity binding partners, and Factor XIIa associated with high affinity binding partners.

23. A method as claimed in any one of claims 1 to 22 wherein the detection or determination is carried under

conditions under which the form or forms of Factor XIIa under investigation is/are not disrupted.

24. A method as claimed in any one of claims 1 to 23 wherein a separation step is carried under conditions under which the form or forms of Factor XIIa under investigation is/are not disrupted.

25. A method as claimed in any one of claims 1 to 24, wherein the form or forms of Factor XIIa is/are detected or determined using immunoassay.

26. A method as claimed in claim 25, wherein the assay is an immunoassay that is capable of detecting or determining the form or forms of Factor XIIa under investigation preferentially relative to other forms of Factor XIIa.

27. A method as claimed in claim 26, wherein the assay comprises the use of an antibody that is capable of binding to the form or forms of Factor XIIa under investigation.

28. A method as claimed in claim 27, wherein the antibody is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa.

29. A method as claimed in claim 27 or claim 28, wherein the antibody is labeled with a label that is detectable directly or indirectly.

30. A method as claimed in claim 29, wherein the antibody is radiolabelled.

31. A method as claimed in any one of claims 25 to 30, wherein a resulting antigen-antibody complex is detected or determined directly.

32. A method as claimed in any one of claims 25 to 31, wherein a resulting antibody-antigen complex is detected by flow cytometry, surface plasmon resonance, surface acoustic wave methodogy or quartz crystal microbalance methodology.

33. A method as claimed in any one of claims 25 to 32, wherein the sample is a tissue sample and the form or forms of Factor XIIa under investigation is/are detected or determined by immunohistology.

34. A method as claimed in claim 27 other than when dependent on claim 5, wherein the antibody is immobilized on a solid phase as a capture antibody.

35. A method as claimed in claim 34, wherein the antibody immobilized on a solid phase as a capture antibody is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa.

36. A method as claimed in claim 35, wherein the capture antibody is mAb 2/215 or an analogue thereof.

37. A method as claimed in claim 35, wherein the capture antibody is mAb 201/9 or an analogue thereof.

38. A method as claimed in any one of claims 34 to 37, wherein the solid phase is contacted with the sample and any resulting antigen-antibody complex is detected or determined using a labeled antibody as defined in claim 28 or claim 29.

39. A method as claimed in claim 38, wherein the labeled antibody is mAb 2/215 or an analogue thereof, mAb 201/9 or an analogue thereof, or a polyclonal antibody that is capable of binding to Factor XIIa.

40. A method as claimed in any one of claims 1 to 39, wherein the parameters of the procedure for detection or determination are adjusted such that the forms or forms of Factor XIIa under investigation is/are detected or determined preferentially relative to other forms of Factor XIIa.

41. A method as claimed in claim 40, wherein the procedure for detection or determination is carried out in the absence of a detergent.

42. A method as claimed in claim 40, wherein the procedure for detection or determination is carried out in the presence of a detergent.

43. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor αXIIa.

44. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor βXIIa.

45. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor βXIIa.

46. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor αXIIa bound to low affinity binding partners.

47. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor βXIIa bound to low affinity binding partners.

48. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor βXIIa bound to low affinity binding partners.

49. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor αXIIa bound to high affinity binding partners.

50. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or

determination of Factor βXIIa bound to high affinity binding partners.

51. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor βXIIa bound to high affinity binding partners.

52. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of molecular complexes incorporating two or more molecules of Factor XIIa.

53. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor XIIa that is bound to cells or cellular derived material.

54. A method as claimed in any of claims 1 to 42, wherein the procedure enables preferential detection or determination of Factor XIIa that is bound to lipids, lipoproteins or remnants thereof.

55. A method as claimed in any of the claims 43 to 53, wherein the immunoassay is a capture assay in which the capture antibody is mAb 2/215 or an analogue thereof and the labeled antibody is mAb 2/215 or an analogue thereof.

56. A method as claimed in any one of claims 1 to 24 other than claim 5 and claims dependent thereon, wherein

the form or forms of Factor XIIa is/are detected or determined using a chromogenic assay.

57. A method as claimed in any one of claims 1 to 56, wherein the sample has been obtained from a subject having a disease or disorder, undergoing a disease or disorder, or after having had a disease or disorder or treatment for the disease or disorder.

58. A method as claimed in claim 57, wherein the disease or disorder involves the coagulation system.

59. A method as claimed in claim 57, wherein the disease or disorder involves hemaocoagulation, fibrinolysis, kininogensis, complement activation or angiogenesis, maintaining vascular wholeness and blood pressure, maintaining the constitutive anticoagulant character of the intravascular space, or tissue defence and repair.

60. A method as claimed in claim 57, wherein the disease or disorder is or involves acute or chronic inflammation, shock of any aetiology including septic shock, diabetes, allergy, a thrombo-haemorrhagic disorder, sepsis, spontaneous abortion or an oncological disease.

61. A method as claimed in claim 57, wherein the disease or disorder is or involves intravascular blood coagulation or thromboembolism, a myocardial infarction, acute coronary syndrome or angina.

62. A method as claimed in claim 57, wherein the disease or disorder is or involves thrombosis or stenosis.

63. A method as claimed in claim 57, wherein the disease or disorder is or involves suspected myocardial infarction or acute coronary syndrome.

64. A method as claimed in claim 57, wherein the disease or disorder is or involves sepsis.

65. A method as claimed in claim 57, wherein treatment involves administration of a therapeutic agent and/or involves a surgical procedure.

66. A method as claimed in claim 65, wherein the treatment is coronary artery angioplasty or thrombolysis.

67. A method as claimed in any one of claims 1 to 66, wherein a series of samples obtained from a subject are tested.

68. A method as claimed in claim 67, wherein samples are obtained during the course of the disease or disorder.

69. A method as claimed in claim 66 or claim 67, wherein samples are obtained during treatment of the disease or disorder, before treatment is started and/or after treatment has finished.

70. A method for diagnosing, monitoring, or predicting the susceptibility to, progress of, or outcome of a disease or disorder, or of treatment of the disease or disorder in a subject having or suspected of having the disease or disorder, which comprises detecting or determining one or more forms of Factor XIIa in preference to other forms of Factor XIIa in a sample obtained from the subject, and comparing the results obtained for the subject with the results obtained using the same assay for samples obtained from at least any one or more of the following:

(i) subjects having the disease or disorder;

(ii) subjects having the disease or disorder, which subjects were monitored in relation to the progress and/or outcome of the disease or disorder;

(iii) subjects having the disease or disorder and the treatment;

(iv) subjects having the disease or disorder and the treatment, which subjects were monitored in relation to the treatment in relation to the progress and/or outcome of the disease or disorder;

(v) subjects who do not have the disease or disorder;

(vi) the same subject before the onset of the disease or disorder or before the start of the treatment of the disease or disorder; and

(vii) the same subject at an earlier or later stage of the disease or disorder or the treatment of the disease or disorder or before the onset of the disease or disorder.

71. A method as claimed in claim 70, wherein the form or forms of Factor XIIa under investigation is/are

detected or determined using a method as claimed in any one of claims 1 to 56.

72. A method as claimed in claim 70 or claim 71, wherein the disease or disorder is as defined in any one of claims 58 to 64.

73. A method as claimed in claim 62 or claim 63, wherein treatment is as defined in claim 65 or claim 66.

74. A method as claimed in any one of claims 70 to 73, wherein the samples are as defined in any one of claims 67 to 69.

75. A method as claimed in claim 70 or claim 71, wherein samples are obtained upon or following admission of the subject to hospital with suspected myocardial infarction, and wherein low levels of particular forms of Factor XIIa are associated with an increased risk of a secondary troponin positive event.

76. A method as claimed in claim 70 or claim 71, wherein samples are obtained upon or following admission of the subject to hospital with suspected myocardial infarction, and wherein high levels of particular forms of Factor XIIa are associated with an increased risk of a secondary troponin positive event.

77. A method as claimed in claim 70 or claim 71, wherein samples are obtained upon or following admission of the subject to hospital with suspected myocardial

infarction, and wherein low levels of particular forms of Factor XIIa are associated with an increased risk of death.

78. A method as claimed in claim 70 or claim 71, wherein samples are obtained upon or following admission to hospital with suspected myocardial infarction, and wherein high levels of particular forms of Factor XIIa are associated with an increased risk of death.

79. A method as claimed in claim 70 or claim 71, wherein high levels of particular forms of Factor XIIa are associated with sepsis.

80. A method comprising carrying out a series of assays for Factor XIIa on samples obtained from subjects having a disease or disorder or treatment for a disease or disorder, and selecting an assay that provides information on Factor XIIa levels that is relevant to the disease or disorder or the treatment.

81. A method for providing an assay for Factor XIIa suitable for providing information relevant for diagnosing, monitoring, or predicting the susceptibility to, progress of, or outcome of a disease or disorder, or of treatment of the disease or disorder in a subject having or suspected of having the disease or disorder, which comprises carrying out a series of assays for Factor XIIa on samples obtained from subjects having the disease or disorder or the treatment, and determining which assay(s) provide information on Factor XIIa levels that is relevant to diagnosing, monitoring, or predicting

the susceptibility to, progress of, or outcome of the disease or disorder, or of treatment of the disease or disorder.

82. A method as claimed in claim 81, comprising comparing the results obtained for Factor XIIa in the samples obtained from subjects having the disease or disorder otr the treatment with the results obtained using the same assay for samples obtained from at least any one or more of the following:
(i) subjects having the disease or disorder;
(ii) subjects having the disease or disorder, which subjects were monitored in relation to the progress and/or outcome of the disease or disorder;
(iii) subjects having the disease or disorder and the treatment;
(iv) subjects having the disease or disorder and the treatment, which subjects were monitored in relation to the treatment in relation to the progress and/or outcome of the disease or disorder;
(v) subjects who do not have the disease or disorder;
(vi) the same subject before the onset of the disease or disorder or before the start of the treatment of the disease or disorder; and
(vii) the same subject at an earlier or later stage of the disease or disorder or the treatment of the disease or disorder or before the onset of the disease or disorder.

83. A method as claimed one of claims 80 to 82, wherein the assay is a method as defined in any one of claims 1 to 56.

84. A method as claimed in any one of claims 80 to 83, wherein the disease or disorder is as defined in any one of claims 58 to 64.

85. A method as claimed in any one of claims 80 to 83, wherein treatment is as defined in claim 65 or claim 66.

86. A method as claimed in any one of claims 80 to 85, wherein the samples are as defined in any one of claims67 to 69.

87. A method as claimed in any one of claims 80 to 86, wherein the results obtained are assembled in a database.

88. A database comprising the results obtained according to a method as claimed in any one of claims 80 to 86.

89. A method comprising detecting or determining Factor XIIa in a sample from a subject, characterised in that the sample is a sample if urine.

90. A method for diagnosing or monitoring a disease or disorder, or monitoring treatment of the disease or disorder, which comprises detecting or determining Factor XIIa in the urine of a subject having or suspected of having the disease or disorder.

91. A method as claimed in claim 90, wherein the disease is or involves renal function, renal disease or renal damage, or treatment therefore.

92. A method as claimed in any one of claims 89 to 91, wherein the results obtained for the subject are compared with the results obtained using the same assay for samples obtained from at least any one or more of the following:

(i) subjects having the disease or disorder, for example, impaired renal function, renal disease or renal damage;

(ii) subjects having the disease or disorder, for example impaired renal function, renal disease or renal damage, which subjects were monitored in relation to the progress and/or outcome of the disease or disorder, for example impaired renal function, renal disease or renal damage;

(iii) subjects having the disease or disorder, for example impaired renal function, renal disease or renal damage and having the treatment therefor;

(iv) subjects having the disease or disorder, for example impaired renal function, renal disease or renal damage and the treatment, which subjects were monitored in relation to the treatment in relation to the progress and/or outcome of the disease or disorder, for example impaired renal function, renal disease or renal damage;

(v) subjects who do not have the disease or disorder, for example impaired renal function, renal disease or renal damage;

(vi) the same subject before the onset of the disease or disorder, for example impaired renal function, renal disease or renal damage or before the start of the treatment of the disease or disorder, for example impaired renal function, renal disease or renal damage; and

(vii) the same subject at an earlier or later stage of the disease or disorder, for example impaired renal function, renal disease or renal damage or the treatment, or before the onset of the disease or disorder, for example impaired renal function, renal disease or renal damage.

93. A method as claimed one of claims 90 to 92, wherein the assay is a method as defined in any one of claims 1 to 56, the sample being urine.